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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/522,134	08/29/2005	Steven Jones	85084-402	3937

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EXAMINER

HURT, SHARON L

ART UNIT	PAPER NUMBER
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1648

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/522,134	Applicant(s) JONES ET AL.	
	Examiner SHARON HURT	Art Unit 1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 December 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3,5,13-15,17-23,25 and 27-31 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3,5,13-15,17-23,25 and 27-31 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on December 30, 2008 has been entered.

Response to Amendment

The amendments to the claims filed December 30, 2008 have been acknowledged and entered. Claims 1-3, 5 and 13 are currently amended.

Status of the Claims

Claims 1-3, 5, 13-15, 17-23, 25 and 27-31 are pending and under examination. Claims 4, 6-12, 16, 24 and 26 have been cancelled.

Claim Rejections - 35 USC § 103

The rejection of claims 1-3, 5, 13-15, 17, 19-23, 25 and 27-31 under 35 U.S.C. 103(a) as being unpatentable over Ito et al. (Journal of Virology, 1999, Vol. 73, No. 10, pages 8907-8912) in view of Kahn et al. (Journal of Virology, 2001, Vol. 75, No. 22, pages 11079-11087) **is withdrawn.**

Applicant's amendments and arguments, filed December 30, 2008, have been fully considered and are persuasive. This obviousness rejection has been withdrawn and new rejections are set forth below.

New Rejections

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-3, 5, 13-15, 17, 19-23, 25 and 27-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ito et al. (Journal of Virology, 1999, Vol. 73, No. 10, pages 8907-8912) in view of Kahn et al. (Journal of Virology, 2001, Vol. 75, No. 22, pages 11079-11087) and Vanderzanden et al. (Virology, 1998, Vol. 246, pages 134-144).

The claimed invention is drawn to a vaccine comprising a recombinant vesicular stomatitis virus (VSV) particle comprising a nucleic acid molecule encoding a viral hemorrhagic fever (VHF) glycoprotein (G) inserted into the viral genome wherein the foreign G has replaced the native VSV G and only the VHF G is expressed on the surface of the recombinant VSV particle, wherein said recombinant VSV particle is infectious, wherein the VHF G is an immunogenic fragment, wherein the VHF G is from Lassa virus, Marburg virus, Ebola virus, Crimean-Congo HFV, Dengue virus, Nipah virus, Hendra virus, Machupo virus, Junin virus, Guanarito virus or Sabia virus, wherein the first gene of the recombinant VSV codes for the VHF G, and further limiting wherein the VHF glycoprotein is from Lassa virus, Marburg virus or Ebola virus.

The claimed invention is drawn to a method of vaccinating an individual comprising administering the VSV particle comprising a VHF G as described above, wherein said recombinant VSV stimulated infection but does not cause disease or symptoms associated with VHF, wherein the particle is administered orally or intranasally.

The claimed invention is also drawn to a method of preparing a pharmaceutical composition for passive immunity comprising said recombinant VSV particle as described above comprising harvesting antibodies from an animal and mixing with a suitable excipient or carrier.

Ito et al. (hereinafter Ito) teaches a recombinant VSV expressing Ebola glycoprotein wherein the mutation reduced the infectivity of the VSVΔG by incorporation of the Ebola virus glycoprotein into recombinant VSV particles (Abstract and page 8908, 2nd column). Ito does not teach a vaccine or a method of preparing a pharmaceutical composition.

Kahn et al. (hereinafter Kahn) teaches a recombinant vesicular stomatitis virus (VSV) expressing foreign proteins that elicit specific protective immunity (Abstract). Kahn teaches the VSV glycoprotein (G) gene was deleted from the full-length cDNA VSV genomic plasmids containing the RSV G gene such that the RSV G genes replaced VSV G in viral genome (page 11081, second column). The RSV G (attachment) is the first and major antigenic glycoprotein (page 11079, last paragraph). Kahn teaches a method of eliciting an immune response in mice by intranasal vaccination with a recombinant VSV expressing RSV G (Abstract). Kahn teaches about vaccine development and passive immunization with a recombinant VSV expressing RSV G (page 11079, last paragraph). Purified RSV was harvested from baby hamster kidney cells and the antibodies were detected by ELISA after mice were inoculated intranasally with recombinant viruses (page 11080, third paragraph and page 11083, second and third paragraph).

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Vanderzanden et al. (hereinafter Vanderzanden) teaches DNA vaccines expressing the envelope glycoprotein (GP) of Ebola virus (EBOV) elicited antibody response and elicited cytotoxic T cell responses (Abstract). Vanderzanden teaches EBOV GP is the most likely viral protein to elicit neutralizing antibodies, because it is the only protein known to be on the virion surface (p. 135, 1st col. 2nd full paragraph). Vanderzanden teaches GP DNA was the most logical vaccine candidate (p. 136, 1st col. 1st full paragraph). Vanderzanden teaches only GP immunized animals were positive in cell proliferation and T cell growth factor assays (p. 140, 2nd col. 1st paragraph).

In summary Ito teaches a recombinant VSV expressing Ebola glycoprotein. Kahn teaches a recombinant VSV expressing a major glycoprotein, a method of replacing VSV glycoprotein with another viral glycoprotein, and a method of eliciting an immune response with the recombinant VSV expressing a foreign glycoprotein. Vanderzanden teaches the Ebola surface glycoprotein is the most logical to use in a vaccine to induce antibodies and elicit an immune response.

It would have been *prima facie* obvious to the person of ordinary skill in the art at the time the invention was made to prepare a vaccine comprising the glycoprotein of a hemorrhagic virus. The person of ordinary skill in the art would have been motivated to make use a VSV expressing the glycoprotein of a hemorrhagic virus to elicit an immune response because Ito teaches it is effective with Ebola (VHF), Kahn teaches how to prepare the composition and Vanderzanden suggests using the glycoprotein. Therefore a person of ordinary skill in the art reasonably would have expected success because of the teachings of Ito, Kahn and Vanderzanden.

Response to Arguments

Applicant's arguments filed December 30, 2008 have been fully considered and will be addressed as they pertain to the new grounds of rejection set forth supra. The arguments in regards to Ito and Kahn have been fully considered but they are not persuasive. Applicants argue “the particles taught by Kahn contain VSV G in addition to RSV F or RSV G.” In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). The particle of Ito only expresses the Ebola glycoprotein (G) and not the VSV G. Applicants argue “Kahn in fact discovered that VSVΔG-RSV G did not induce an immune response or protective immunity although VSVΔG-RSV F did.” The Examiner fails to see the relevance of this argument because RSV is not a VHF virus. Applicants argue “Kahn teaches that VSVΔG-RSV G cannot elicit a protective immune response but that VSV-RSV G can.” Again the Examiner fails to see the relevance of this argument because RSV is not a VHF virus. Applicants argue “one of skill in the art would on considering Kahn in its entirety remember that the VSVΔG-RSV F did not produce neutralizing antibodies and decide that a VSV – VHF construct was far more likely to be successful as a vaccine”. As summarized above it would be obvious to vaccinate with a recombinant VSVΔG-VHF G as taught by Ito and Kahn and suggested by Vanderzanden.

Applicants argue “infectivity alone does not guarantee propagation and propagation does not guarantee an immune response let alone vaccination.” In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the

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features upon which applicant relies (i.e., propagation) are not recited in the rejected claim(s).

Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The claimed invention as claimed does not require a propagating virus. Applicants argue "it is unclear what incentive or motivation there would be to substitute the Ebola GP for RSV G in the VSVΔG construct without supplying VSV G in trans". The motivation is provided by the teachings of Ito whom successfully illustrated that Ebola G can be substituted for the VSV G. In addition, it would be easier if the G was not provided in trans therefore it would have been obvious to a person of skill in the art to try the method without providing the G in trans.

With regard to the strict construction and application of the TSM test, Applicant is directed to *KSR v. Teleflex, Inc.*, No. 04-1350 (U.S. Apr. 30, 2007), which states, "rejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness. As our precedents make clear, however, the analysis need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ." (*KSR*, slip op. at 14). The Court continued, stating that "helpful insights, however, need not become rigid and mandatory formulas; and when it is so applied, the TSM test is incompatible with our precedents. The obviousness analysis cannot be confined by a formalistic conception of the words teaching, suggestion, and motivation, or by overemphasis on the importance of published articles and the explicit content of issued patents." *KSR*, slip op. at 15.

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As such, the rejection at issue and its analysis under 103(a) meets all of the *prima facie* requirements under *Graham v. Deere* (1966) (*supra*) and *KSR v. Teleflex* (2007) (*supra*).

Applicants argue “Combining Ito as suggested by the examiner to substitute Ebola GP for RSV G would still require that VSV G be supplied in trans and even with VSV G being supplied in trans, Kahn teaches that when RSV G was used in the VSV ΔG constructs even with VSV G being supplied in trans, no immune response was obtained.” The examiner disagrees because Ito shows infectivity without VSV G as illustrated in Fig. 4 (p. 8910). Applicants argue “Combining Ito which showed that Ebola GP could be used to confer infectivity to VSVΔG constructs with Kahn possibly suggests that Ebola GP could be substituted for VSV G and supplied in trans.” The Kahn reference is relied upon to teach that it was known in the prior art how to substitute the glycoprotein in the VSV vector with a foreign glycoprotein to induce an immune response. Again, Applicants are arguing the references individually wherein Ito is the primary reference which is more closely related to the instant invention and Kahn is used to support the method of preparing the vector expressing the glycoprotein.

Applicants argue “the inventors have discovered that a VSVΔG particle can be constructed which has only a VHF glycoprotein and no VSV glycoprotein that can be used safely as a vaccine based on its ability to propagate.” Again, Applicants are arguing limitations that are not present in the instant claims and it is known in the art that vaccines prepared with killed viruses which so not propagate are safe vaccines.

Conclusion

No claims allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHARON HURT whose telephone number is 571-272-3334.

The examiner can normally be reached on M-F 8:00 - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Sharon Hurt

February 24, 2009

/Bruce Campell/

Supervisory Patent Examiner, Art Unit 1648